REMARKS

The claims have been amended to insert the limitation of claim 21, thus deleting as unnecessary a phrase objected to by the Examiner. Claim 1 has also been amended to make the optional last step non-optional since it is only the offspring of the crossing of the fourth generation with an immunocompromised rodent that does not express GFP that the capability of further breeding is assured. No new matter has been added and entry of the amendment is respectfully requested.

This amendment obviates the rejections under 35 U.S.C. § 112 and 35 U.S.C. § 102. The remaining rejection, under 35 U.S.C. § 103 is over the combination of Kern (WO02/28188) in view of Okabe, *et al., FEBS Ltrs.* (1997) 467:313-319.

The present claims require that the transgenic rodent must express a fluorescent protein in all tissues except hair and erythrocytes, while maintaining its immunized phenotype, and must be able to breed further. Respectfully, Kern does not teach such a mouse with or without a β actin promoter, and Okabe does not teach immunocompromised rodents at all. For this reason, these documents, even when combined, do not teach the claimed rodent.

Applicants have found that in order to obtain a stable rodent of this type, all four crossings that are set forth in the claim are necessary. Thus, as set forth in Example 1, the first generation, which is the only generation obtained according to the disclosure in Kern, produces only two rare GFP *nu/nu* mice. These mice are relatively unstable, and cannot be continuously used to breed succeeding generations of mice that can be reliably depended upon to breed true to stable fluorescent immunocompromised mice. Applicants have found that the offspring of the fourth crossing, which crossing involves a rodent that does not express the fluorescent protein, but is immunocompromised,

produces rodents that are sufficiently viable and stable to reliably breed additional rodents that are both fluorescent and immunocompromised. The ability to obtain such stably breeding offspring is itself surprising in view of the burden placed on the mouse by both immunocompromising it and making it express the fluorescent protein.

Of course, Kern makes no such disclosure since Kern never actually produced any mice, and therefore only postulates that the first generation would be successful, which it is not. The last step in claim 1, which is now no longer optional, reflects the stability of the rodents obtained through this more elaborate process than disclosed by Kern.

In view of this, applicants believe that the combination of Kern with Okabe fails to render the present invention obvious, since the invention requires sufficient crossings to result in the stable rodent required, and such successive crossings are not described in Kern.

Conclusion

Since Kern simply postulates the obtention of *nu/nu* mice that produce fluorescent proteins or other markers, and has not actually done any work, Kern fails to disclose that in order to obtain such rodents that are stable and capable of reliable reproduction the steps set forth in claim 1 are required. Accordingly, the invention as claimed is not suggested by the combination of Kern with Okabe. The remaining rejections under 35 U.S.C. §§ 112 and 102 have been addressed by amendment. Accordingly, applicants believe that claims 1-3 are in a position for allowance and respectfully request that claims 19 and 20 be rejoined as dependent on allowable claims.

Should minor issues remain that could be resolved by telephone, a telephone call to the undersigned is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 312762004400.

Respectfully submitted,

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